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RECENT AND FORTHCOMING MEETINGS

1949	
26-28 September	WHO Regional Committee for South-East Asia, second session, New Delhi
26-28 September	Joint OIHP/WHO Study-Group on African Rickettsioses, first session, Paris
26 September-5 October	WHO Expert Committee on the Unification of Pharmacopoeias, fifth session, Geneva
10-20 October	WHO Expert Committee on Venereal Infections, third session, Washington, D.C.
12-15 October	WHO Regional Committee for the Eastern Mediterranean, second session, Geneva
12-20 October	WHO Expert Committee on Venereal Infections : Subcommittee on Serology and Laboratory Aspects, Washington, D.C.
24-28 October	Joint FAO/WHO Expert Committee on Nutrition, Geneva
24-29 October	Joint OIHP/WHO Study-Group on African Schistosomiasis, first session, Cairo
18-19 November	Joint OIHP/WHO Study-Group on Cholera, third session, New Delhi
1-6 December	WHO Yellow-Fever Panel, first session, Geneva
5-14 December	WHO Expert Committee on International Epidemiology and Quarantine, second session, Geneva
12-14 December	Joint ILO/WHO Committee on the Hygiene of Seafarers, first session, Geneva
1950	
6-30 January	WHO Executive Board : Standing Committee on Administration and Finance, Geneva
9-14 January	WHO Expert Committee on Drugs Liable to Produce Addiction, second session, Geneva
16 January-2 February	WHO Executive Board, fifth session, Geneva
6-11 February	WHO Expert Committee on Professional and Technical Education of Medical and Auxiliary Personnel, first session, Geneva
20-26 February	WHO Expert Committee on Nursing, first session, Geneva
February, tentatively	Joint ILO/WHO Committee on Industrial Hygiene, first session, Geneva
February, tentatively	WHO Expert Committee on Health Statistics : Subcommittee on Cancer Registration
February, tentatively	WHO Expert Committee on Health Statistics : Subcommittee on the Definition of Stillbirth and Abortion
6 March	WHO Regional Committee for Europe, first session, Geneva
20 March, tentatively	WHO Expert Committee on Health Statistics : Subcommittee on Hospital Statistics
11-15 April	Expert Committee on Antibiotics, first session, Geneva
17 April, tentatively	WHO Expert Group, Meeting on Prematurity, Geneva
20 April, tentatively	WHO Expert Committee on Health Statistics, second session
20-29 April	WHO Expert Committee on the Unification of Pharmacopoeias, sixth session, New York
8 May	Third World Health Assembly, Geneva

NEW DEVELOPMENTS IN VENEREAL-DISEASE CONTROL

Third Session of the Expert Committee on Venereal Infections

Technical considerations were the principal concern of the WHO Expert Committee on Veneral Infections when it met for its third session,[1] held in Washington from 10 to 20 October 1949. The committee discussed control techniques, antibiotic therapy in syphilis and other treponematoses, serological and laboratory aspects of venereal infections, and the report of the WHO Syphilis Study Commission to the USA.

Treponematoses

Although major effort in WHO's venereal-disease programme is to be concentrated on early infectious syphilis and prenatal and infantile syphilis, several developments have made imperative a broader consideration of the entire group of treponematoses. Of these developments, most important is the evidence that the various treponematoses—syphilis, yaws, pinta, and bejel—respond to penicillin treatment. This seems to substantiate the hypothesis of Hudson [2] that the treponemal diseases,

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[1] The following took part in this session :

Members :

Dr W. E. Coutts, Professor of Venereology ; Chief, Department of Social Hygiene, Public Health Administration, Santiago, Chile
Dr R. Degos, Professeur agrégé à la Faculté de Médecine de Paris, France
Dr S. Hellerstrøm, Professor of Dermato-syphilology, University of Stockholm, Sweden
Dr E. H. Hermans, Medical Director, Association for the Combating of Venereal Diseases, Rotterdam, Netherlands
Dr J. F. Mahoney, Chief, Laboratory of Antibiotic Research and Development, Section of Laboratory of Infectious Disease, Microbiological Institute, National Institutes of Health (US Public Health Service), Staten Island, N.Y., USA (*Chairman*)
Dr G. L. M. McElligott, Director, Venereal Disease Department, St. Mary's Hospital ; Adviser in Venereal Diseases, Ministry of Health, London, United Kingdom *(Rapporteur)*
Dr I. H. Nagi, Director, Venereal Diseases Section, Ministry of Public Health, Cairo, Egypt
Dr R. V. Rajam, Professor of Venereology, Government General Hospital, Madras, India (*Vice-Chairman*)

Co-opted Consultants :

Dr N. R. Ingraham, Chief, Division of Venereal Disease Control, Department of Public Health, Philadelphia, Pa., USA
Dr P. V. Marcussen, Physician in charge, Venereal Disease Clinic, Kommunehospitalet, Copenhagen, Denmark ; Chairman, WHO Syphilis Study Commission to the United States
Dr E. W. Thomas, Professor of Clinical Medicine, New York University College of Medicine ; Director, Rapid Treatment Center, Bellevue Hospital, New York City, N.Y., USA

Observers :

Dr G. E. Samame, Venereal Disease Consultant, Pan American Sanitary Bureau, Washington, D.C., USA
Dr P. Sanchez, Chief, Venereal Disease Division, Department of Health, Caracas, Venezuela
Dr W. F. Snow, President, International Union against Venereal Diseases, New York City, N.Y., USA
A. Woodchek, International Labour Office, Washington, D.C., USA

Secretariat :

Dr T. Guthe, Chief, Venereal Diseases Section, WHO (*Secretary*)
Dr A. Spillmann, Regional Adviser on Venereal Diseases for Europe, WHO

Dr M. Grzybowski, Professor of Dermatology, Director, Clinic of Dermatology and Syphilology, University of Warsaw, Poland, was unable to attend.

[2] Hudson, E. H. (1946) *Treponematoses*, New York

including syphilis, are caused by closely related organisms but exhibit varying clinical and epidemiological patterns in different parts of the world, possibly because of environmental factors.

The success of mass application of penicillin in "eradication projects" against yaws and syphilis in parts of Africa, certain Pacific islands, and the USA has encouraged WHO support of the campaign against yaws which is part of the United Nations technical assistance to Haiti.[3] The Expert Committee on Venereal Infections welcomed this project as an

FIG. 1. EXPERT COMMITTEE ON VENEREAL INFECTIONS, THIRD SESSION

Front row, left to right: Dr E. H. Hermans; Dr R. Degos; Dr G. L. M. McElligott (Rapporteur); Dr R V. Rajam (Vice-Chairman). Middle row, left to right: Dr J. F. Mahoney (Chairman); Dr I. H. Nagi; Dr S. Hellerstrøm; Dr T. Guthe (WHO); Dr W. E. Coutts. Back row, left to right: Dr P. V. Marcussen; Dr A. Spillmann (WHO)

opportunity to demonstrate the effectiveness of control programmes based on penicillin in a large-scale campaign in a geographically delimited area with a high prevalence of disease. It recommended that procaine penicillin G in oil with 2% aluminium monostearate be the form of penicillin employed.

A second significant development is the treponemal antibody technique introduced by Nelson,[4] which permits study of the biological and immu-

[3] A report on the mission to Haiti will be published in a forthcoming number of the *Chronicle*.

[4] See page 42.

nological relationship between the causative agent of the various treponematoses in man and animals, a distinction which cannot be made with classical serological methods.

A third important technical consideration is the recent support given to the identification of bejel as an endemic syphilitic disease. The committee recommended that the bejel project in the Eastern Mediterranean area should get under way early in 1950.[5] This project, proposed by the Director-General of WHO and adopted by the Regional Committee for the Eastern Mediterranean, calls, in the first place, for a survey to be carried out by a special team of 3 or 4 experts who would explore the epidemiological, clinical, and laboratory aspects of bejel. Next would be the selection by this team of a special demonstration area where a disease-eradication campaign based on penicillin and modern case-finding techniques could be carried out. On the basis of experience gained in the demonstration area, it would be possible to proceed with a broad campaign against bejel over a wide area. Concomitant with the control programme would be comparative laboratory studies, particularly on the trepenomes of syphilis and bejel. It was the opinion of the Expert Committee on Venereal Infections that the pilot area for field and laboratory investigations should be established in Iraq as soon as the hot season is over.

It is felt that WHO can make a significant contribution to the ultimate definition of the nature of treponemal diseases in man and of their biological and immunological relationships by utilizing the clinical and laboratory material available in field units and national laboratories in areas where treponematoses are prevalent. The disease-eradication campaigns against yaws and syphilis in Haiti and against bejel in the Eastern Mediterranean area will be a step in this direction.

Two considerations of an administrative nature were brought to the attention of the Expert Committee on Venereal Infections:

1. The referring of treponematoses other than syphilis to the Expert Committee on Venereal Infections by the Executive Board and the World Health Assembly.

2. The decision of the Second World Health Assembly to establish in 1950 an Expert Committee on Treponematoses, to be composed of 9 members, including 3 syphilis experts of the present Expert Committee on Venereal Infections.[6] The latter recommended that the terms of reference of the new committee be clarified so as to avoid duplication of effort, or that WHO consider merging the two committees in 1951. Also recommended was the establishment of appropriate study-groups or subcommittees as required.

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[5] *Off. Rec. World Hlth Org.* **15**, 29 ; **17**, 11

[6] *Off. Rec. World Hlth Org.* **21**, 27

Serodiagnosis

Of major importance in any venereal-disease activity is to have uniform, effective, and practical means of serodiagnosis. At the present time there is little uniformity in the methods used, and comparisons of reactions are not always valid. The same method may give different reactions in the same patient because of differences in the material or in the technique employed. There are numerous other complicating factors, chief among which are:

1. Unreliability of test methods under different climatic conditions. Test methods which are reliable in temperate climates often fail under tropical conditions.

2. Impracticality of some of the most reliable techniques. Procedures which are very elaborate and expensive have limited use, particularly in mass screening activities under field conditions.

3. Limited manufacture of cardiolipin antigens. Technical difficulties and the patent protection for the production of cardiolipin lecithin make the wide use of this means of serodiagnosis very difficult at present.[7]

Although the situation with regard to serodiagnosis is unsatisfactory, the committee did not want their observations to be taken as a complete invalidation of present methods. The problem becomes one of trying to improve serodiagnostic methods. According to the committee, " the most promising development in this regard is the introduction of the immobilizing antibody technique (Nelson and Turner); . . . The differentiation between what appear to be true and non-specific reagins employing this technique may in future prove of fundamental importance in the serodiagnosis of syphilis ".

The committee recommended that the Subcommittee on Serology and Laboratory Aspects, the report of which is discussed elsewhere in this issue,[8] proceed with its programme for the establishment of an international antigen reference standard, study the possibility of recommending a uniform test procedure to all countries, and consider setting up international reference centres for making control sera and antigens available to national laboratories.

Antivenereal Drugs and Therapy

A survey recently made by WHO shows that penicillin consumption is likely to increase progressively in all parts of the world, whereas production will probably remain limited, for some time, to Europe and America.[9] The Expert Committee on Venereal Infections considered this

[7] See page 44.
[8] See page 41.
[9] *Chron. World Hlth Org.* 1949, 3, 292

survey incomplete, however, and recommended that the study be continued.

The committee discussed the use of repository penicillin preparations, which have greatly simplified penicillin therapy.[10] A single injection of 300,000 Oxford units of procaine penicillin with 2% aluminium monostearate can maintain an effective blood level for about 96 hours. Penicillin treatment in dosages of 600,000 to 2,400,000 units has special significance in cases of early infectious syphilis. The committee recommended that sufficient time has not yet passed to evaluate with certitude the ultimate results of this penicillin treatment. However, it is remarkable that, in observations made during the last two years, there do not appear to have occurred any completely acceptable instances of central nervous system relapse in patients who received adequate penicillin therapy in the early stages of infection. This gives hope that the danger of development of syphilis of the central nervous system may pass and that the prolonged post-treatment follow-up, which is presently necessary, may be curtailed and a shorter routine adopted.

Recognizing the epidemiological value of penicillin, the committee considered that its use on a large scale should be organized as part of public-health activities in areas with a high prevalence of treponemal disease. To compare its efficacy with older methods of treatment, a group of three members of the committee will report at a subsequent meeting on suitable case material treated with (*a*) arsenicals and/or bismuth, and (*b*) penicillin preparations.

With regard to the *Pharmacopoea Internationalis*, now being prepared by an expert committee of WHO,[11] it was suggested that the characteristics of vehicles and water-repellent substances used in penicillin preparations be included in the *Pharmacopoea*. Standardization of repository preparations is essential if comparative investigations are to be valid. The committee also considered that the following drugs should be included in the *Pharmacopoea Internationalis*:

Arsenoxides
Aureomycin
Neoarsphenamine
Procaine penicillin G
Sodium penicillin G
Streptomycin
Sulfadiazinum
Sulfaguanidinum
Sulfathiazolum

Maritime Aspects

The committe made specific recommendations regarding these questions, calling attention to the desirability of more countries' adhering to the Brussels Agreement pending the establishment of wider interna-

[10] See Thomas, E. W. (1949) *Bull. World Hlth Org.* **2**, 233.
[11] *Chron. World Hlth Org.* 1949, **3**, 279

tional regulations for venereal-disease control and to the need for liaison with the Joint ILO/WHO Committee on the Hygiene of Seafarers.

Study Commission to USA

The committee expressed the opinion that the interim report of the WHO Syphilis Study Commission to the United States represents a significant contribution which many health administrations, institutions, and workers in the venereal-disease field will wish to have as a reference document. The results obtained by the Commission will be summarized in a forthcoming issue of the *Chronicle*. The report itself will be published shortly as *World Health Organization: Technical Report Series*, no. 15.

Developments and Perspectives

In setting forth long- and short-term objectives for WHO's venereal-disease activities, the committee emphasized the following points:

1. Priority should be given to economically underdeveloped areas with a high prevalence of syphilis and/or other treponematoses.

2. WHO should continue its advisory and demonstration services and should stimulate training of personnel in the field. The facilities in demonstration areas can be used effectively in training programmes.

3. Venereal-disease control activities should be integrated with other public-health programmes, particularly those relating to general disease prevention and to maternal and child health. Pregnancy care provides an opportunity for case-finding not only among mothers but also among other members of families. Mass examinations for malaria and tuberculosis also aid in finding cases. Antisyphilitic programmes should be combined with measures against other treponematoses where these are prevalent. An effort should be made to initiate activities which can continue to operate after outside assistance is withdrawn.

4. WHO should continue to assemble and distribute venereal-disease literature to health administrations and other institutions concerned. The rapidity of technical developments in the therapeutic and laboratory aspects of venereal-disease control make it difficult for research and field workers in all countries to be adequately informed. WHO's services as a clearing-house and distribution centre for venereal-disease literature have significant value.

The report on this session of the Expert Committee on Venereal Infections will be published as *World Health Organization: Technical Report Series*, no. 13.

SEROLOGY OF SYPHILIS

The Subcommittee on Serology and Laboratory Aspects (of the Expert Committee on Venereal Diseases) devoted the major part of the discussions at its first session,[1] held in Washington from 12 to 20 October 1949, to the question of the International Serological Laboratory Conference which the World Health Organization proposes to convene in 1951 or 1952. Similar conferences took place in 1923 and 1928 at Copenhagen and in 1930 at Montevideo. The war prevented the holding of one in Copenhagen in 1939, as had been planned. In 1941 a conference for the Western hemisphere met in Washington. It was of great benefit to the subsequent development of research in the USA and laid the foundation for further standardization work in the serology of syphilis.

Need for an International Conference

The need to hold a new laboratory conference is making itself urgently felt. The fact is, as was stressed by the subcommittee, that present techniques for the serodiagnosis of syphilis lack uniformity; different methods of reporting the results of serological tests lead to confusion and render valueless many of the studies published in the past on the serology of syphilis. The present position is such that an individual may be declared syphilitic in one country and free from the disease in another.

There are, in addition, other factors emphasizing the need for an international serodiagnostic laboratory conference. New serological tests have been introduced into practice in the USA and elsewhere during recent years, but many countries have not yet tried them out. Some of these tests employ antigen components of a much higher degree of chemical purity than the ones previously used. This is particularly true in the case of antigens containing cardiolipin and purified lecithin, which have been found more sensitive and more specific than antigens prepared with less

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[1] The following took part in this session:

Members :

A. Harris, Senior Serologist, Venereal Disease Research Laboratory (US Public Health Service), Staten Island, N.Y., USA

Dr P. Krag, Assistant Director, Serodiagnostic Department, State Serum Institute, Copenhagen, Denmark (*Chairman*)

Dr R. Laporte, Chef du Service de la Sérologie, Institut Pasteur, Paris, France

Dr I. N. Orpwood Price, Director, Venereal Diseases Reference Laboratory (Public Health Laboratory Service), St. Peter's Hospital, London, United Kingdom (*Vice-Chairman*)

Consultants and Advisers :

Dr P. V. Marcussen, Physician in charge, Venereal Disease Clinic, Kommunehospitalet, Copenhagen, Denmark

Dr T. B. Turner, Professor of Bacteriology, School of Hygiene and Public Health, Johns Hopkins University, Baltimore, Md., USA

Dr M. V. Veldee, Medical Director, Hyland Laboratories, Los Angeles, Cal., USA (Member of WHO Expert Committee on Biological Standardization)

Secretariat :

Dr T. Guthe, Chief, Venereal Diseases Section, WHO (*Secretary*)

Dr A. Spillmann, Regional Adviser on Venereal Diseases for Europe, WHO

The report on this session will be published shortly as *World Health Organization : Technical Report Series*, No. 14.

pure extracts. The advances made in this field open up the possibility of establishing a durable reference antigen standard. It is clear that developments of the greatest interest are possible in this direction.

Furthermore, a new method has been evolved which arouses great hopes among serologists, namely Nelson's treponemal antibody technique.[2] According to this technique, the serum of syphilitic rabbits and of persons in whom the disease has proceeded beyond the primary stage immobilizes virulent *Treponema pallidum* and causes it to lose its power of infecting the rabbit. This immobilization, which develops only in the presence of complement, appears to be due to a specific antibody which is different from and independent of the reagin detected in ordinary serological tests. As may be imagined, Nelson's technique opens up great possibilities in the immunology of syphilis. Moreover, as pointed out by the subcommittee, it could play an important part in the interpretation of false positive reactions.

Finally, there is an important reason, in addition to the above technical grounds, for organizing this conference on a world scale. Investigations so far made show that in certain areas, particularly in the tropics, seropositive reactions are extremely frequent; furthermore, the frequency varies according to the type of test used in serodiagnosis. It follows that the evaluation of the tests and choice of reactions adapted to the various areas represent a problem which should be tackled on a world scale. Consequently, it will be necessary to obtain for the conference sera originating in different parts of the world. The subcommittee therefore appealed to all important laboratories to collaborate.

General Plans for the Conference

After unanimously recognizing the need for an international conference on serological techniques, the subcommittee took up the practical side of its organization, which it discussed in its broad outlines. Various suggestions were examined concerning the date, place, number of participants, general programme of work, etc. In the view of the subcommittee, the conference should be convened in a city which is an important medical centre and which has an airport served by one or more world airlines, so as to ensure the transport of samples of sera coming from different parts of the world in the minimum time. Laboratories should be chosen so as to offer the best working conditions to the greatest possible number of authors of tests. London, Paris, or Copenhagen would fulfil these various conditions. The number of methods which would be demonstrated at the conference is estimated to be about 40. They should be selected on a purely technical basis, the demonstrations being given by the author of the method or by workers designated by him.

[2] Nelson, R. A. & Mayer, M. M. (1949) *J. exp. Med.* **89**, 369

The subcommittee was of the opinion that tests should be run on at least 3,000 sera, at the rate of 200 a day, and on 250 samples of spinal fluid, at the rate of 16 per day.

The categories of sera with which the tests would deal would be the following :

Normal sera : About 1,500 samples taken from individuals not showing any morbid symptoms—but not a serologically pre-selected group—coming from at least three geographical areas.

Abnormal, non-syphilitic sera : About 500 samples taken from individuals suffering from malaria, leprosy, herpes genitalis, from patients who are febrile owing to disease, from pregnant women, etc. ; about 300 samples of sera giving false positive reactions and also complying with various definite conditions.

Syphilitic sera : About 1,000 samples taken from individuals suffering from primary, secondary, or tertiary syphilis of whom only a part have received appropriate treatment. The number of recent untreated cases should not be below 100.

Spinal fluid : Samples from subjects without syphilitic symptoms and from syphilitics in whom the central nervous system has not been affected.

National Centres for Serodiagnosis

Other problems dealt with during the session are also indirectly connected with the projected conference, particularly co-operation between laboratories or national centres in the reciprocal evaluation of performance of tests and the exchange of information.

Samples of sera and antigens intended for serodiagnosis have already been exchanged between laboratories in Bulgaria, Denmark, Ethiopia, Finland, France, Italy, and the United Kingdom and the Venereal Disease Research Laboratory of the US Public Health Service, which acted as reference centre. These exchanges were found to be so fruitful that they might well be established on a more systematic basis. This system should be extended to national laboratories in all WHO regions. Such exchanges of information between laboratories might also make useful contributions to the methods of conserving sera, particularly those which give false positive reactions ; present knowledge on this subject is very limited.

The subcommittee suggested that WHO draw the attention of national health-administrations to the necessity of establishing in each country a laboratory or national centre for the serodiagnosis of syphilis to participate in action taken in this field on an international scale.

Other Questions

After having examined various questions relating to the projected conference, the subcommittee proceeded to deal with several other subjects.

In particular, it studied the problem of cardiolipin, that of bejel and the other treponematoses, considered from the serological viewpoint, and the various problems raised by the technique of mass serological examinations.

Cardiolipin

The use of antigens based on cardiolipin-lecithin had been advocated by the Expert Committee on Venereal Diseases during its second session [3] in an effort to encourage the standardization of serological tests for the diagnosis of syphilis.

There are two important obstacles to the general use of cardiolipin : the technical difficulties encountered in large-scale production of this substance and the fact that its manufacture is protected by a patent. The latter, which is held by the New York State Department of Health, was established not for commercial purposes, but to ensure the purity of the cardiolipin products. It has been suggested that WHO administer this patent internationally. The subcommittee considered that, if the administration of international patents were not within the province of WHO, the problem could be approached in another way: the possibility of establishing an international cardiolipin reference standard might be considered in conjunction with the Expert Committee on Biological Standardization, should developments in this field indicate this to be advisable. A high degree of purity of cardiolipin is essential to ensure the accuracy of serological tests employing antigens containing cardiolipin and purified lecithin. Consequently, the current purity control tests for this substance should be studied by the subcommittee.

Bejel, syphilis, and other treponematoses

Thanks to technical improvements made during the last two years, it is now possible to obtain sufficiently concentrated and pure suspensions of treponemata, i.e., without tissular impurities, for the study of various serological problems connected with the immunology of syphilis, false positive reactions, and the relationships, both biological and immunological, between the various strains of treponemata. The members of the subcommittee had an opportunity, thanks to the courtesy of the Department of Bacteriology, Johns Hopkins School of Hygiene and Public Health, Baltimore, to become acquainted with research on treponemal antibodies and particularly with the new treponemal antibody technique.

Several interesting points were brought to light by the comparative study of the different techniques.

The titre of the immobilizing antibody (Nelson's antibody) is generally high in syphilis; at times it is distinctly at variance with the reagin titres obtained by the lipoid antigen method. After specific treatment, the Nelson

[3] *Off. Rec. World Hlth Org.* **15**, 24; *Bull. World Hlth Org.* 1949, **2**, 146

antibody persists longer than the reagin. Finally, there is the particularly striking fact that the Nelson test has been consistently negative in all cases of undeniably false positive reactions. Furthermore, the Nelson technique has made it possible to differentiate strains of *T. pallidum* and *T. pertenue*.

These results promise developments of the greatest interest. On the one hand, as pointed out by the subcommittee, the treponemal antibody technique enables a different approach to be made to the study of false positive reactions and perhaps to elucidate their nature. On the other hand, it may make it possible to study the various strains of treponemata with reference to their biological and immunological inter-relationships.

The programme for the control of bejel will enable interesting experiments in this field to be made in the near future. This WHO project for a campaign against bejel in the Eastern Mediterranean region, where this disease represents an important public-health problem, met with the approval of the subcommittee. From the serological viewpoint, various investigations could be undertaken in which the new techniques would play a part. The results obtained would increase present knowledge of bejel and throw light on the problem of the other treponematoses. These studies would be concerned with the following points:

(*a*) serological relationship between bejel and syphilis;

(*b*) nature and extent of bejel;

(*c*) experimental infection of the rabbit with the bejel treponema;

(*d*) immunity and cross-immunity in experimental treponematoses (syphilis, pinta, yaws, bejel).

Mass serological examinations

The general application of mass serological examinations has shown the acute nature of certain serological problems, such as false reactions —both positive and negative—the drawbacks attached to the use of a single test for diagnosis, etc. To these technical questions are added problems of a practical nature, e.g., pressure of work in laboratories which have to carry out thousands of flocculation or complement-fixation tests daily, the inadequate equipment of laboratories in underdeveloped areas, etc.

The subcommittee noted various practical experiences, particularly the satisfactory results obtained by the WHO venereal-disease demonstration team at Simla in Northern India [4] with a modified Meinicke test, used in conjunction with a cardiolipin test.

On the basis of this preliminary information, the subcommittee recommended that techniques suitable for mass examinations be studied and that the results and the statistical data collected by the demonstration teams be assembled and submitted to the subcommittee at its next session.

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[4] *Chron. World Hlth Org.* 1949, 3, 294

ANOTHER STAGE IN PREPARATION OF INTERNATIONAL SANITARY REGULATIONS

Second Session of the Expert Committee on International Epidemiology and Quarantine

The new international sanitary regulations are intended to standardize and replace the existing international conventions, particularly those of 1926, 1933 and 1938, which were drawn up by delegates at the Office International d'Hygiène Publique (OIHP), and were modified in 1944 by UNRRA.[1]

Under Article 21 (*a*) of its Constitution, WHO is responsible for carrying out this task, which, when accomplished, will provide a means for ending the confusion resulting from the adherence of various countries to conflicting sanitary conventions. The need for revising the old regulations is particularly urgent because certain quarantine restrictions are of doubtful value and hinder international communications. Moreover, certain health-administrations have a tendency to demand information, for example, vaccination certificates, the value of which is now questioned.

The basic principles of the new international sanitary regulations were laid down by the Expert Committee on International Epidemiology and Quarantine in November 1948.[2] The preamble and the commentary on the basic principles were written by Dr Dujarric de la Rivière.[3] The final text, with the amendments suggested by the expert committee, was approved by the Second World Health Assembly.[4]

Since then considerable progress has been made. The Expert Committee on International Epidemiology and Quarantine, at its second session, held in Geneva from 5 to 14 December 1949,[5] revised the draft international sanitary regulations, which will enter into force after the final text has been approved by the World Health Assembly. WHO will then have accomplished a work of paramount importance, which will have a considerable effect on international relations.

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[1] Dujarric de la Rivière, R. (1948) *Prophylaxie nationale et internationale des maladies épidémiques*, Paris, p. 231

[2] *Off. Rec. World Hlth Org.* **19**, 7; *Chron. World Hlth Org.* 1949, **3**, 1

[3] *Off. Rec. World Hlth Org.* **19**, 12

[4] *Off. Rec. World Hlth Org.* **21**, 22, 328; *Chron. World Hlth Org.* 1949, **3**, 194

[5] The following took part in this session:

Members:

Dr R. Dujarric de la Rivière, Sous-Directeur de l'Institut Pasteur. Paris, France
Dr G. L. Dunnahoo, Medical Director, Chief, Division of Foreign Quarantine (US Public Health Service), Washington, D.C., USA
Dr G. D. Hemmes, Inspector of Public Health, Utrecht, Netherlands
Dr M. D. Mackenzie, Principal Medical Officer, Ministry of Health, London, United Kingdom
Dr J. D. McCormack, Deputy Chief Medical Adviser, Department of Health, Dublin, Ireland
Dr M. T. Morgan, Président du Comité permanent de l'Office International d'Hygiène Publique; Port of London Authority, London, United Kingdom (*Chairman*)
Dr M. Nazif Bey, Under-Secretary of State, Ministry of Public Health, Cairo, Egypt
Dr K. C. K. E. Raja, Director-General of Health Services, New Delhi, India

Compilation of the Draft International Sanitary Regulations

The drawing-up of the text of the draft international sanitary regulations, as submitted to the Executive Board, was made possible by carrying out extensive preliminary investigations and by referring to the most recent scientific data. The latter were supplied by the work of the expert committees and study-groups on cholera, yellow fever, plague, insecticides, and environmental sanitation, which has been reported in the *Chronicle*. Other fundamental work had already been carried out, particularly on smallpox, on the inspection of anti-yellow-fever vaccine, bills of health, etc.,[6] and on improving the system of epidemiological notification.[7] Consequently, it was possible to study the draft of the revised international sanitary conventions in the light this fresh knowledge had thrown on the epidemiology, etiology, and prophylaxis of pestilential diseases. All this new information, acquired during recent years, clearly shows that many articles in the old conventions are now out of date or invalid.

In addition to the work that has been mentioned, the expert committee considered draft international sanitary regulations drawn up by its chairman, Dr M. T. Morgan, in collaboration with Dr M. Gaud, Directeur, Office International d'Hygiène Publique. This study also included draft supplementary regulations to be applied to the Red Sea area during the season of the Mecca pilgrimage. Various suggestions and observations concerning the revision of the conventions were also made by governments and by the International Civil Aviation Organization. These comments may be divided into four classes: (1) general observations; (2) observations connected with an article in the draft regulations; (3) observations relating to the pilgrimage; (4) observations referring to sanitary conditions in connexion with the movements of certain groups of travellers. The expert committee also noted the recommendations made, on its behalf,

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Dr G. H. de Paula Souza, Director and Professor, Faculty of Hygiene and Public Health, University of São Paulo, Brazil

Representative of the United Nations :

P. de Bellaigue, Division of Transports and Communications, Lake Success, N.Y., USA

Observers :

ICAO:

R. J. Moulton, Chief, Facilitation Section, International Civil Aviation Organization, Montreal, Canada

Dr F. de Tavel, Medical Adviser, International Civil Aviation Organization, Montreal, Canada

OIHP:

Dr M. Gaud, Directeur de l'Office International d'Hygiène Publique, Paris, France (*Rapporteur, Joint OIHP/WHO Study-Groups*)

PASB:

Dr F. L. Soper, Director, Pan American Sanitary Bureau; and Director, WHO Regional Office for the Americas, Washington, D.C., USA

Secretariat :

Dr Y. M. Biraud, Director, Division of Epidemiology, WHO (*Secretary*)

Dr W. Omar, Epidemiologist, WHO Regional Office for the Eastern Mediterranean, Alexandria, Egypt

Dr G. Stuart, Chief, Sanitary Conventions and Quarantine Section, WHO (*Secretary, Section on Quarantine*)

Dr W. W. Yung, Director, WHO Epidemiological Intelligence Station, Singapore

Dr H. S. Gear, Deputy Chief Health Officer for the Union of South Africa, Cape Town, Union of South Africa, was unable to attend.

[6] *Chron. World Hlth Org.* 1947, **1**, 146; 1948, **2**, 137, 252, 255

[7] *Chron. World Hlth Org.* 1948, **2**, 36; 1949, **3**, 35, 92

FIG. 2. EXPERT COMMITTEE ON INTERNATIONAL EPIDEMIOLOGY AND QUARANTINE, SECOND SESSION - I

Left to right : Dr F. L. Soper (PASB) ; Dr M. T. Morgan (Chairman) ; Dr Y. M. Biraud (WHO) ; Dr G. Stuart (WHO)

by the following WHO expert committees and study-groups which met during 1949: Expert Committee on Insecticides (10-15 May), Expert Committee on Plague (19-24 September), Joint OIHP/WHO Study-Group on Cholera (18-19 November), and Yellow-Fever Panel (1-6 December).

Yellow Fever

Before the meeting of the Expert Committee on International Epidemiology and Quarantine, the Yellow-Fever Panel met in Geneva from 1 to 6 December 1949, to determine the present position of yellow fever with regard to quarantine and preventive measures. Their findings have been summarized elsewhere in this issue.[8]

Plague

Among the factors considered in connexion with quarantine measures against plague, the following should be mentioned specially: the delimitation of endemic areas, the possibility of exterminating reservoirs and vectors of plague in seaports and airports, the preventive treatment of pneumonic plague, and the possibility of disinfesting rice. The report

[8] See page 52.

on the first session of the Expert Committee on Plague formed a basis for the study of these subjects.[9]

Cholera

The study of endemic areas and that of the connexion between epidemic outbreaks of cholera is continuing. In India, endemic areas have already been defined, and many factors causing the endemicity of cholera in that country have now been ascertained. The Joint OIHP/WHO Study-Group on Cholera made recommendations concerning the elimination of the endemic foci at a later stage.[10]

Environmental Sanitation

It is obvious that water pollution, lack of food hygiene, the presence of insect or animal vectors of communicable diseases, and other deficiencies with regard to sanitation favour the spread of pestilential diseases. It follows therefore that WHO, by its work on environmental sanitation, can play an important part in exterminating these diseases. In fact, as

FIG. 3. EXPERT COMMITTEE ON INTERNATIONAL EPIDEMIOLOGY AND QUARANTINE, SECOND SESSION - II

Left to right (seated round table) : Dr F. de Tavel (ICAO) ; P. de Ballaigue (United Nations) ; Dr G. H. de Paula Souza ; Dr M. Gaud (OIHP) ; Dr K. C. K. E. Raja ; Dr R. Dujarric de la Rivière; Dr F. L. Soper (PASB)

[9] *Chron. World Hlth Org.* 1949, 3, 269
[10] *Chron. World Hlth Org.* 1950, 4, 20

Dr H. S. Gear stated in a document submitted to the committee, " quarantine barrier methods are of very limited value and . . . resistance of a community to infection is dependent upon its internal conditions ".

Insecticides

The Expert Committee on Insecticides [11] gave technical advice on international specifications for insecticides and on the design of spraying equipment. Standard methods for the disinsection of ships and aircraft were also suggested. The role of insecticides in the control of flies was studied, as well as the measures necessary to prevent the introduction of anophelines into non-infested areas.

Revised Draft International Sanitary Regulations

The revised text of the draft international sanitary regulations, which has been presented to the Executive Board, will be passed to Member States and to interested international organizations for comments and will then be submitted to the World Health Assembly for final approval. The regulations will be put into force during the six months after this final approval has been given. The draft, as amended by the Expert Committee on International Epidemiology and Quarantine, contains a list of definitions of the special sanitary and epidemiological terms mentioned in section I. The second part comprises the articles dealing with the maritime and aerial conventions. The sanitary regulations applicable to the Red Sea area during the season of the Mecca pilgrimage are contained in a separate document, which also provides information on the safety and sanitary standards necessary for the protection and welfare of the pilgrims during transport by sea and air.

Once they have been adopted, the WHO regulations relating to the international control of epidemics should remain in force for a fixed period, such as five years, without amendment, so that the confusion which would be caused by frequent changes may be avoided and also to enable the officials responsible for their application to become familiar with the regulations. For this reason, the committee was of the view, despite the opinion expressed by the First World Health Assembly, that the clauses relating to the sanitary inspection of the Mecca pilgrimage should not be incorporated in the basic regulations.

Second Session of the Quarantine Section

The Section on Quarantine of the Expert Committee on International Epidemiology and Quarantine—composed of Dr Dunnahoo (Chairman),

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[11] *Chron. World Hlth Org.* 1949, 3, 153

Dr Mackenzie, Dr Nazif Bey, Dr de Paula Souza, and Dr Raja—met in Geneva on 13 December 1949. Since the first meeting,[12] about twenty complaints had been submitted by governments regarding measures imposed by other governments in excess of the provisions of the present international sanitary conventions. The Section on Quarantine noted that the Secretariat had dealt adequately with the majority of these problems. At this meeting, other questions were also considered; as a result, the validity of certificates for inoculation against yellow fever, issued in the prescribed manner by military doctors, was recognized, and the right of every government to prescribe the disinsection treatment it considers necessary for aircraft was acknowledged. Travellers coming from an area free from *A. aegypti* and visiting a sanitary airport in a yellow-fever area on their way to an area considered to be exposed to infection, i.e., infested with *A. aegypti*, should not, in the opinion of the Section on Quarantine, be obliged to produce a certificate of inoculation against yellow fever. If, however, there is some doubt as to whether the sanitary airport is infested with *A. aegypti*, the certificate, if demanded, should have a duration of validity identical with that prescribed by the International Sanitary Convention for Aerial Navigation, 1944, that is, from ten days to four years after the date of inoculation. Finally, with regard to deratting certificates, it was decided that, if seven months had elapsed since a deratting certificate was issued, the health authority of the port in question would have the right to submit a ship to further deratting.

The report on the second session of the Expert Committee on International Epidemiology and Quarantine, as well as that of the Section on Quarantine, will be published shortly as *World Health Organization: Technical Report Series*, no. 20.

[12] *Chron. World Hlth Org.* 1949, 3, 7

YELLOW FEVER AND ENDEMIC AREAS

Members of the Yellow-Fever Panel met in Geneva from 1 to 6 December 1949 [1] to advise the Expert Committee on International Epidemiology and Quarantine, which is responsible for drafting the new WHO sanitary regulations for the five pestilential diseases (plague, cholera, yellow fever, typhus and smallpox). The experts examined the present position regarding yellow-fever endemicity with a view to making the preventive and quarantine measures as tolerable as is consistent with the protection of public health.

In South America, and especially in Brazil, as reports presented to the panel by Dr W. S. Sá Antunes and Dr F. L. Soper clearly show, intensive campaigns, in conjunction with the Pan American Sanitary Bureau, with insecticides with residual action, have led to the elimination from urban centres of the yellow-fever vector, *Aëdes aegypti*. These achievements made it possible to envisage, in the near future, the disappearance of this mosquito from the entire country.

The position in Africa is less satisfactory. The panel recommended that campaigns should be undertaken in this continent for the extermination of the yellow-fever vector and that WHO should provide technical and financial assistance to any health authorities concerned who might desire it. It is possible, however, that such campaigns can be carried out successfully only in those areas where *Aëdes aegypti* is not a forest-dwelling mosquito.

Enzootic and Endemic Yellow Fever

The progressive destruction of *Aëdes aegypti* in South America has reduced the danger of urban epidemics to a minimum and makes it possible to contemplate the eradication of yellow fever from all inhabited areas. It is impossible, however, to expect the final and complete disappearance of this disease. It does, in fact, exist in enzootic form among certain jungle animals (jungle yellow fever) in areas where *Aëdes aegypti* is not present and where it may, nevertheless, occasionally be transmitted to man (woodcutters, hunters, etc.). This possible source of infection, therefore, must always be borne in mind when considering the epidemiology of yellow fever.

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[1] The following were present:

Members:

Dr W. S. Sá Antunes, Director, National Yellow Fever Service, Ministry of Education and Health, Rio de Janeiro, Brazil

Dr G. L. Dunnahoo, Medical Director, Chief, Division of Foreign Quarantine (US Public Health Service), Washington, D.C., USA

Dr A. F. Mahaffy, formerly Director, Yellow Fever Research Institute, Entebbe, Uganda (*Chairman*)

Médecin-Colonel G. Saleun, Adjoint technique du Directeur du Service de Santé colonial, Ministère de la France d'Outre-Mer, Paris, France

Secretary:

Dr G. Stuart, Chief, Sanitary Conventions and Quarantine Section, WHO

Dr Y. M. Biraud, Director, Division of Epidemiology, WHO, and Dr F. L. Soper, Director, Pan American Sanitary Bureau, and Director, WHO Regional Office for the Americas, Washington, D.C., USA, also attended.

The report on the session will be published shortly as *World Health Organization: Technical Report Series*, no. 19.

FIG. 4. YELLOW-FEVER PANEL, FIRST SESSION

Left to right : Dr F. L. Soper (Regional Director, WHO) ; Médecin-Colonel G. Saleun ; Dr A. F. Mahaffy (Chairman) ; Dr W. S. Sá Antunes ; Dr G. L. Dunnahoo

Observations made in South America over a period of many years show that it is possible to distinguish four types of areas where yellow fever exists:

(1) *enzootic areas*, where *Aëdes aegypti* is not present, but where the virus exists and persists among animals for long periods, causing, from time to time, accidental cases in man ;

(2) *epizootic areas*, in which *Aëdes aegypti* is not present, but where the disease appears in animals from time to time for short periods;

(3) *endemic areas*, in which *Aëdes aegypti* is present, and where the virus exists and remains for long periods, and where its transmission from man to man is therefore possible;

(4) *epidemic areas*, in which human cases due to the transmission of the virus by *Aëdes aegypti* occur.

Delimitation of Endemic Areas

The endemic areas, to which quarantine measures are permanently applied, were delimited by UNRRA in 1946, [2] as laid down by the International Sanitary Convention for Aerial Navigation, 1944. It now devolves

[2] *Chron. World Hlth Org.* 1948, **2**, 232

upon WHO to give practical effect to this delimitation on the lines of the recommendations of the Yellow-Fever Panel. These recommendations are based on various criteria :

For America, they are based on reported clinical cases, on the results of the systematic examination of liver specimens taken from all persons dying after a febrile illness lasting ten days or less, on immunity tests carried out with human and animal sera, and on the *Aëdes aegypti* index.[3]

For Africa, they are based mainly on the results of immunity tests.

The delimitation set up in 1946 was re-examined during this session, and the panel suggested various modifications. In all cases where towns and ports are excluded from endemic areas, the condition was expressly made that the *Aëdes aegypti* index should not exceed 1 % and that a quarterly report on the subject should be sent to WHO. A zero index is desirable, and has been attained in South American ports.

America

The panel considered that the port of Manaos (Brazil) should be excluded from the endemic area. On the other hand, the rural areas of the whole Republic of Panama and of the Panama Canal Zone (excluding the ports) should be included therein.

Africa

The endemic area, which extends from latitude 15°N. to latitude 10°S., i.e., over almost the whole of tropical Africa, should be left as originally defined by UNRRA until, as was the case of South America, further research on the distribution of the virus and its vectors permits more exact determination of the yellow-fever endemic areas in this vast territory. It would then be possible to adapt quarantine measures more exactly to cover the actual risks of infection. Nyasaland and the territory to the south of Barotseland lying between longitudes 23°E. and 25°E. and as far as latitude 21°S. should be incorporated in the endemic area. On the other hand, conditions at the port of Jibuti (French Somaliland) are such that it may be excluded. In its request for exemption, the French Government pointed out that not a single case of yellow fever had been observed in the town for 55 years and that very strong measures have been taken by the health services to ensure effective control throughout the whole of the surrounding territory.

Certificates of Inoculation against Yellow Fever

After specifying various measures to be taken in connexion with sanitary conditions at airports and quarantine measures applicable to aircraft,

[3] The *Aëdes aegypti* index gives the percentage of dwellings, that is, of habitations occupied by a single family, in which *Aëdes aegypti* larvae are found. Computation of the index is to be based on an examination of all dwellings in a port, city, or area.

ships, and other vehicles, as well as to the passengers, the experts examined the question of certificates of inoculation against yellow fever. They felt that the certificates should be recognized as valid from the tenth day to the end of the sixth year following inoculation. These figures ensure an adequate safety margin, since it has been shown that effective immunity becomes established as early as the seventh day after inoculation and that it lasts more than six years.

Furthermore, the experts suggested that the certificate of immunity against yellow fever introduced by UNRRA be abolished. In point of fact, the International Sanitary Convention of 1944, amending that of 1926, provided that a certificate of immunity could be accepted instead of an inoculation certificate. This certificate of immunity had to be issued by an approved laboratory to persons recognized as being immune as the result of an attack of yellow fever. However, it is practically never requested by those concerned. Moreover, it is impossible for laboratories to distinguish the immunity established as a result of inoculation from that conferred by the disease; finally, there is no known contraindication to the inoculation of immune persons. For all these reasons, abolition of the certificate of immunity seems to be justified.

MALARIA CONTROL IN ISRAEL

Professor G. G. Mer, Chief, Antimalaria Service of the Government of Israel, and Director, Malaria Research Station, Rosh Pina, has reported the results obtained since 1945 by the malaria-control campaign to the WHO Eastern Mediterranean Regional Committee, which met in Geneva from 12 to 15 October 1949, and to the Expert Committee on Malaria.

Among the Jewish population in the Israel portion of Palestine, consisting of old settlers and new immigrants, the incidence of malaria was 1,207 in 1945, 466 in 1946, and 226 in 1947. During this period the population was 600,000. In 1948 the population increased by 150,000, and 1,227 new cases of malaria were recorded.

The methods used in malaria control have been gradually expanded since 1945, through the application of DDT and the use of proguanil (paludrine). DDT has been applied as a larvicide and insecticide. Proguanil has been used since 1948 as a clinical suppressive agent.

In his report Professor Mer makes some observations on these different methods of malaria control. He is of the opinion that a 1—2.5% solution of DDT in kerosene is very effective as a larvicide, provided the application is repeated every 15 days during the summer. A 5% solution of DDT in kerosene, sometimes with 0.5% sesame oil added, was used for disinsecting dwellings, 1 g. of DDT applied per square metre. It was found that the

application of DDT as an insecticide effected a decrease in the occurrence of *Anopheles sacharovi*, but a similar reduction was not observed in the case of *A. superpictus* or *A. sergentii*.

Suppressive treatment with proguanil proved effective and is capable of checking a malaria epidemic in 2 weeks if the individual doses of the drug are adequate, that is, 0.2 g. administered twice a week. Doses of 0.1 g. were insufficient for preventing all cases of falciparum infection and for suppressing all vivax infections. The curative effect of proguanil in both falciparum and vivax infections was generally poor compared to that of quinine or mepacrine taken with or without plasmoquine.

Reports from WHO Fellows

Many of the letters and reports received from WHO Fellows have been of such interest that they deserve to be read by a wider public. They demonstrate more vividly than a series of facts and figures both the character of the fellowship programme and the response of the Fellows themselves. Selections from these reports have therefore been published from time to time, but it must be emphasized that the opinions expressed therein are those of the Fellows themselves.

Production of BCG at Copenhagen

Dr G. A. Villarreal, Chief of the BCG Clinical Control Service of the National Committee for the Control of Tuberculosis in Mexico, has had an opportunity of studying the production of BCG at the State Serum Institute, Copenhagen. In the report he has submitted, Dr Villarreal describes the various stages of production and stresses the care taken by the institute to obtain a high-quality vaccine.

In view of the fact that BCG cannot either be heated or mixed with an antiseptic, it has to be prepared with the utmost care in order to avoid contamination and to ensure that its potency is stable and adequate. The BCG Department of the State Serum Institute, Copenhagen, takes every possible precaution to achieve this. Before engagement, the staff undergo a thorough chest examination which is repeated every three months. They are forbidden to enter the laboratories where work is in progress on virulent strains of tubercle bacilli. The whole of the staff works with a sense of responsibility, observing the strictest discipline and the most rigorous aseptic rules.

The vaccine is prepared in a special building apart from the rest of the institute, and the animals used for testing are likewise isolated. Equipment is carefully sterilized and is subjected to strict inspection. The room where the vaccine is prepared is provided with eight ultraviolet lamps, for an area of 5m. × 5m., which give an adequate sterility margin to the whole room. These lamps are always switched on for 15 minutes before any work is begun.

The vaccine prepared at the institute is intended for intradermal administration. It contains 0.75 mg. of bacilli per millilitre of diluted Sauton medium. It is prepared once a week and is stored in a refrigerator at a temperature of 2° to 4° C.

The strain of BCG which is used in the State Serum Institute was obtained from the Institut Pasteur, Paris, in 1931. During the first 10 years the culture was subcultured in bile-potato broth with transfers to glycerine-potato broth and finally to liquid Sauton medium. At the present time, subculturing is usually carried out directly in Sauton's medium, the transfer to bile-potato broth being made only after 100 to 150 passages through the former medium.

The vaccine itself is prepared from the cultures in Sauton's medium. The age of the culture has a great influence on the potency of the vaccine. If the culture is young, the potency of the vaccine will be low. If, on the other hand, it is old, the potency will be even lower, owing to the presence of many dead bacilli. Fourteen days seem to be the optimum growing-period, for the cultures then contain the highest number of living bacilli. Before the vaccine is prepared, the cultures are examined to make certain that the liquid is clear; the bottles containing the cultures are then shaken and their contents are poured into a filter (Birkhaug apparatus). The mass of bacilli is pressed by the piston of the apparatus and has the appearance of an almost dry cake. After various operations have been performed, the culture is weighed and is then transferred to a sterile Fernbach flask containing 2.5 kg. of stainless-steel balls of 4-mm. diameter. The quantity of BCG obtained is usually between 5 and 10 g. per flask. The flasks are then placed in an electric rotator which revolves at 40 r.p.m., in order to disintegrate the mass of bacilli and produce a homogeneous suspension; 20 ml. of diluted Sauton medium are then added. The duration and speed of the rotation have an effect upon the quality and potency of the vaccine. If the rotation is of too short duration, the emulsion will still contain lumps. If, on the other hand, it is continued for too long, the bacilli will be impaired and partly destroyed and the resulting vaccine will have a low potency. The optimum time of rotation is six minutes. In order to obtain the stock suspension, a sufficient quantity of diluted Sauton medium is added until the suspension contains 40 mg. of bacilli per millilitre. From this suspension the vaccine is prepared by adding diluted Sauton medium so that the liquid finally contains 0.75 mg. of bacilli per millilitre. It is then put into ampoules.

At various stages during its production the vaccine is submitted to a sterility test (for aerobic and anaerobic micro-organisms). The potency of the vaccine is then estimated, since being a suspension of living bacilli the vaccine cannot be standardized. It follows, therefore, that production of the vaccine at its various stages must be made as uniform as possible if a stable potency is to be obtained. The ideal vaccine is one that can cause anergic persons to react to the tuberculin test without giving rise to any complications. If the vaccine contains less than 0.75 mg. of bacilli per millilitre, it will have a low potency. It will give a less certain immunity, and for a shorter period, than the normal vaccine. Should it contain more bacilli per millilitre, its potency will be greater. A vaccine with a very high potency may cause strong local reactions, such as abscesses, which, although not serious, may in the long run discredit BCG. The BCG department therefore recommends that great care should be taken to weigh the bacilli as accurately as possible. For this, the cultures must be dried sufficiently before being weighed. Four dilutions of the vaccine, in decreasing strengths, are tested by inoculation into four white guinea-pigs, each weighing 450 grams. The local reactions after intradermal inoculation should be measured twice a week, and this observation should be continued until the nodules have disappeared.

From the very beginning of the production of BCG, innocuity tests have been carried out systematically on guinea-pigs at the Copenhagen institute, with the object of detecting both virulent tubercle bacilli and other pathogenic organisms. These tests have shown that BCG is a stable organism which is unable to give rise to general tuberculosis.

The content of viable bacilli in the vaccine is determined from the number of colonies appearing on Löwenstein's medium after six weeks of incubation. The homogeneity of the suspension is also examined.

The laboratory is kept informed by the antituberculosis dispensary of the reactions to, and results of, BCG inoculations. Dr Villarreal himself was able to perform most of the tests which he describes in his interesting report.

WHO Publications

Epidemiological and Vital Statistics Report

Contents of numbers of the *Report* published since the last listing [1] follow :

Vol. 1, No. 18 (November 1948). " Malaria in Europe, 1938-1947 ", by E. Pampana. Table : Malaria

Vol. 1, No. 19 (December 1948). " The declining death-rate ", by K. Stowman. Tables : General death-rates in some countries; General death-rates in large towns; Tuberculosis mortality.

Vol. 2, No. 1 (January 1949). " Syphilis and gonorrhoea in Germany ", by T. Guthe. Tables : Syphilis; Gonorrhoea (gonococcal infections).

Vol. 2, No. 2 (February 1949). " The 1948/49 influenza wave in Europe ", by G. Stuart. Tables : Influenza; Undulant fever; Relapsing and tick fevers.

Vol. 2, No. 3 (March 1949). Tables : Birth-rates in some countries; Birth-rates in large towns; Infant mortality rates in some countries; Infant mortality rates in large towns.

Vol. 2, No. 4 (April 1949). " Evolution of mortality in Europe during the twentieth century ", by M. Pascua. Table : Smallpox.

Vol. 2, No. 5 (May 1949). Tables : Cholera; Yellow fever; Typhus fever; Dysentery.

Vol. 2, No. 6 (June 1949). Tables : Whooping cough; Diphtheria.

Vol. 2, No. 7 (July 1949). Tables : General death-rates in some countries; General death-rates in large towns; Tuberculosis mortality.

Vol. 2, No. 8 (August 1949). " Prevalence of plague in the world in recent years ", by P. M. Kaul. Table : Plague.

Vol. 2, No. 9 (September 1949). Tables : Measles; Scarlet fever; Cerebrospinal meningitis.

Vol. 2, No. 10 (October 1949). " Deaths by cause, sex and age in Europe ", by M. Pascua (with detailed tables).

Official Records of the World Health Organization

Two numbers of the *Official Records* were published in December 1949 :

No. 21. Second World Health Assembly. This number is divided into three parts. Part I contains the decisions and resolutions adopted; Part II contains the report of the proceedings, subdivided into verbatim records of the plenary meetings, minutes of the General Committee and main committees, and committee reports; Part III contains 24 annexes comprising detailed reports on specific subjects, notes and comments submitted by delegations, texts of agreements, etc.

No. 22. Report of the Executive Board, fourth session. In addition to the report on the work of this session, and relevant annexes, this number contains, in the form of a supplement, reports on the three sessions of the Joint Committee on Health Policy, UNICEF/WHO.

[1] *Chron. World Hlth Org.* 1949, 3, 19

Notes and News

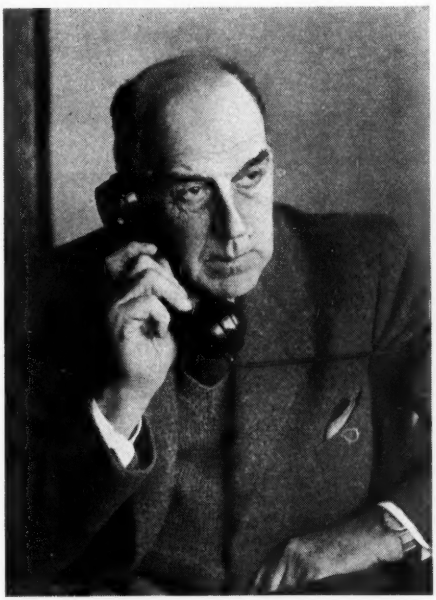
Dr Raymond Gautier Leaves WHO

At the beginning of this year Dr R. Gautier retired from the post of Assistant Director-General of WHO. In March he will assume the functions of Research Director for the International Children's Centre in Paris.

Dr Gautier was born in Geneva on 7 January 1885. After graduation as Doctor of Medicine from the University of Basle, he was appointed assistant in the Institute of Pathological Anatomy of that University in 1918, and first assistant in the Laboratory of Physiology, University of Geneva, in 1920. He received the Bizot award for his research on the cerebrospinal fluid and, specifically, for having enunciated the concept of the " blood-brain barrier ".

In 1923 and 1924 he was Chief of Operations at the Institut d'Hygiène et de Bactériologie, University of Geneva. It was there that he undertook original research on, among other subjects, bovine fluorosis in relation to the emanations of aluminium works.

FIG. 5. Dr R. GAUTIER



In 1924 Dr Gautier joined the Health Organization of the League of Nations, where he was concerned with biological standardization. From 1926 to 1930 he occupied the post of Director of the Eastern Office, League of Nations Health Organization, at Singapore. He took an active part in combating the cholera outbreak at Shanghai in 1928 and in establishing a radio epidemiological information service. He was also the initiator of a series of epidemiological and immunological studies.

After his return to Geneva in 1930, he devoted his full time to biological standardization for the next eight years. The two studies which he published in 1935 and 1946 provide a résumé of all that had been done in this field and are considered as reference works of permanent value.[1]

In 1939 he was appointed Acting Director of the Health Section of the League of Nations, in which post he remained until 1942. From then until the end of the war, Dr Gautier was entrusted with a series of important missions to London and Washington for the purpose of organizing health measures in liberated Europe.

When the Interim Commission of the World Health Organization was established in 1946, Dr Gautier was appointed Counsellor and, later, Director of the Geneva

[1] *Quart. Bull. Hlth Org. L.o.N.* 1935, **4**, 497; *Bull. Hlth Org. L.o.N.* 1945, **12**, 1

Office. In 1948 he became Assistant Director-General of the permanent Organization

Dr Gautier is the author of numerous medical works dealing specifically with questions relating to the epidemiology of scarlet fever and cholera, to pituitary tumours, peroral vaccination, tropical pneumonia, preventive vaccination of dogs against rabies, bacteriophages, etc. He is a Member of the Senate of the Académie suisse des Sciences médicales and Honorary Member of the Epidemiological Section of the Royal Society of Medicine, London.

The International Children's Centre in Paris, where Dr Gautier will continue his career, is a new foundation of the French Government which, according to its statutes, has as its objective the promotion, in the different countries of the world, of the study of problems pertaining to infancy, the propagation of knowledge on hygiene and child welfare, and the technical training of specialized personnel. The centre is available to the specialized agencies and services of the United Nations, as well as to various national institutions for the protection of mothers and children.

In announcing his colleague's departure to the WHO Executive Board, Dr Brock Chisholm, WHO Director-General, said : " We are losing a loyal, co-operative, and highly skilled colleague ". The Executive Board unanimously expressed its deep appreciation of Dr Gautier's long and eminent service in international health and especially of his work in the World Health Organization.

World Health Day

The Second World Health Assembly decided that World Health Day should be observed on the anniversary of the entry-into-force of the WHO Constitution following its ratification by 26 States Members of the United Nations (7 April 1948). Various suggestions have been made by the WHO Director-General to governments regarding the organization of programmes for this day. The list of suggestions has been drawn up partly on the basis of reports from various countries regarding programmes organized in 1949.

The theme which has been proposed by the Director-General for 1950 is " Know Your Own Health Services ". This theme brings together the national and international aspects of public-health work. It will encourage people to study their own health problems and the services which are coping with them, will assist them to determine what contribution they themselves can make towards improving their health, and will enable them to become informed concerning the work being carried out by national health authorities and by WHO.

The celebration of World Health Day might possibly be combined with the special health days or health weeks which some countries devote to health problems; all that would be necessary would be to have the two celebrations coincide.

An information kit containing background material to serve as a basis for organizing World Health Day programmes is being prepared. Among the suggestions already sent to governments is information on the co-operation which national health administrations can obtain from different institutions and associations, educational centres, the press, radio, etc.

Two Women Specialists Appointed WHO Expert Consultants

Two women specialists who have been appointed expert consultants of the World Health Organization left Geneva on 19 December 1949 to carry out the tasks with which they have been entrusted. They are Dr Pearl Kendrick, chief of the Western Michigan Laboratory, one of the branches of the Department of Health of Michigan, and Mrs Lucia Moholy, formerly Director, Aslib Microfilm Service, Victoria and Albert Museum, London.

Dr Kendrick went to London, at the request of the United Kingdom Ministry of Health, to assist in organizing mass-vaccination campaigns against whooping cough. This disease presents serious problems in Britain, where it causes more deaths among children than does diphtheria: in England and Wales 748 fatal cases were registered in 1948 and 217 were recorded in the first quarter of 1949. Dr Kendrick is the first WHO expert whose services have been requested by the United Kingdom.

Mrs Moholy has visited Prague, to collaborate with the Czechoslovak Government in establishing documentation and microfilm services at the State Medical Library. Once these services are organized, they will be available to other countries of eastern Europe.

Venereal Diseases

India

A number of points in the December 1949 report of the WHO venereal-disease demonstration team in India,[1] are of interest.

First of all, the proportion of sero-positivity is remarkably high, the adult rate being about 70%. Cases of syphilis in the early, infective, stage are numerous. Cases of clinically diagnosed granuloma inguinale are more common in women. It is interesting to note that cases of acute gonorrhoea in men are rare. The general state of health of the population is precarious and reveals the lack of medical attention.

On 3 December the programme of mass treatment in the Ghund area was completed. Those suffering from syphilis had been given procaine penicillin G in oil with 2% aluminium monostearate. The response of the people themselves deserves comment. Although they had been informed by the authorities of the details of the campaign and the benefits they might derive from it, they were very suspicious. Hence, at the start, there were not many patients. The results of treatment, in those suffering from early syphilitic lesions, or even common impetigo, became apparent about the third day, so that confidence was rapidly established. From then on, the population showed its approval by flocking to the treatment centre. Dr J. Kvittingen, returning to the area one month after the campaign had started, was unable to discover any fresh case of venereal disease, whereas previously some 15 to 20 new cases were detected every month.

Finland

A venereal-disease specialist Dr M. Tottie, of Stockholm, has left Geneva for Helsinki, where he will take part in the anti-venereal-disease campaign that has been launched in Finland by the United Nations International Children's Emergency Fund (UNICEF) and WHO. He is to make a special study of the methods of treatment and prevention of congenital syphilis.

Inoculation and Vaccination Certificates

WHO has recently published a *List of Countries' Inoculation and Vaccination Certificate Requirements*, as on 1 December 1949.[2]

There is no provision in the international sanitary conventions now in force for making vaccination or inoculation against plague, cholera, yellow fever, typhus, or smallpox compulsory. However, for some years, such certificates have been demanded by certain countries from travellers coming from infected, suspect, or even healthy areas. An investigation undertaken by WHO in September 1948 among the health administrations of every country has enabled data to be obtained from 108 countries or territories.

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[1] See *Chron. World Hlth Org.* 1949, **3**, 294

[2] Supplement to the *Wkly Epidem. Rec.* 1950, **25**, No. 2. This publication may be obtained from the World Health Organization, Sales Section, Palais des Nations, Geneva, price 1 Swiss franc, post-free.

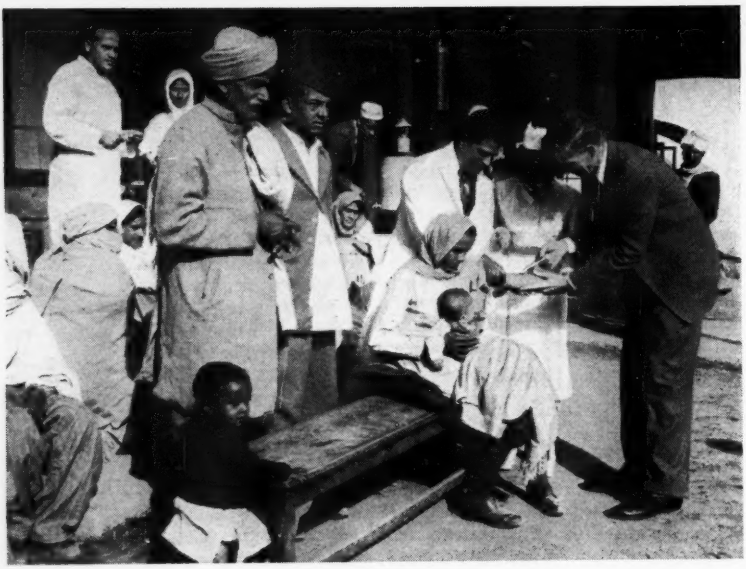

FIG. 6.
WHO VENEREAL-DISEASE DEMONSTRATION TEAM IN INDIA - I

Taking blood samples from patients at a rural hospital near Simla

FIG. 7. WHO VENEREAL-DISEASE DEMONSTRATION TEAM IN INDIA - II

Giving an anti-venereal-disease injection

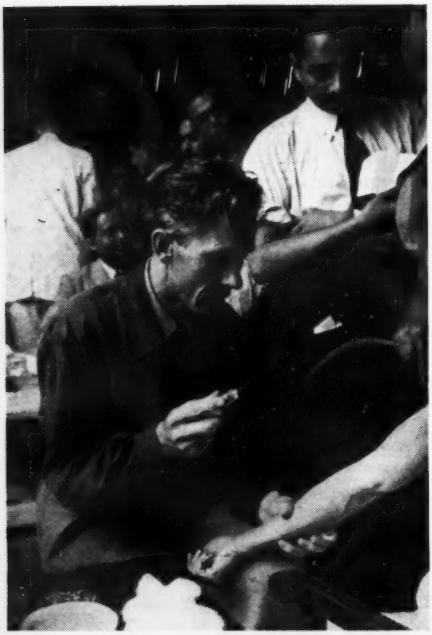

FIG. 8. WHO VENEREAL-DISEASE DEMONSTRATION TEAM IN INDIA - III

Taking a blood sample.
Left : Dr J. Kvittingen (team serologist)

It is obvious that WHO does not necessarily approve of all the measures that have been enforced. Its aim is simply to make known the existing state of affairs.

The position will doubtless be modified after the publication of the new WHO international sanitary regulations, which have recently been drafted by the Expert Committee on International Epidemiology and Quarantine.[1]

Training for Antituberculosis Work in Turkey

An antituberculosis training-centre is to be set up in Turkey with the assistance of WHO. Dr E. Berthet, tuberculosis officer of the Department of Isère, France, has been made responsible for the organization of the centre, which will be concerned with prophylaxis, with methods of diagnosis, and with the treatment of tuberculosis. Equipment will be provided by WHO. The setting-up of this centre will mark the launching of a large-scale programme of tuberculosis control in Turkey.

WHO Sends Nurses to Borneo and Korea

Five nurses left Geneva on 23 January 1950 for Borneo and Korea. They will assist in carrying out maternal and child health programmes.

Miss I. Simmons and Miss P. Scanlan are going to Brunei, while Mlle H. Wenger and Miss O. Warren have been posted to Sarawak; both these territories are situated in the north-west of the island of Borneo.

Mlle W. Visscher is going to South Korea and will form part of a team headed by Dr E. Leppo, a member of the WHO Secretariat.

Poliomyelitis in India

In order to check the epidemic that has broken out in India, a team of WHO specialists in the treatment and rehabilitation of poliomyelitis victims has left for that country.[2] The team is made up of Dr N. Kezerian, Assistant Resident Orthopaedic Surgeon, Johns Hopkins Hospital, Baltimore, USA, Mrs H. Kezerian, a nurse at the same hospital, and Miss S. A. Bruton, a physiotherapist attached to the Maryland League of Crippled Children.

Homeless Children

Dr J. Bowlby, Director of the Child Guidance Department of the Tavistock Clinic, London, has been appointed by WHO to study the problem of homeless children. Dr Bowlby left Geneva on 16 January 1950 for Paris, Amsterdam, and Stockholm, where he will visit various institutions and reception centres. He will collect scientific data on the effects of loss of parents or home on the mental health of children.

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[1] See page 46.

[2] See *Chron. World Hlth Org.* 1949, 3, 292.

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